Cu^{2+}- treated plants. In both organs, the decrease of auxin-dependent gene expression was found, which can partly explain the growth inhibitions.

In plant organs, Cu^{2+} treatment results in severe morphological responses during which the endogenous hormonal balance and signal transduction are affected. Auxin and NO negatively regulate each other's level and NO intensifies the metal-induced cotyledon expansion, but mitigates elongation processes under short-term Cu^{2+} exposure. Besides hormonal system, nitric oxide metabolism was also influenced by copper. In the root tips, this heavy metal excess induced NO generation, while NO content in lateral roots was not affected by the treatments. Using *nia1nia2* mutants, nitrate reductase enzyme as a putative source of Cu^{2+}-induced NO was identified in *Arabidopsis* primary roots.

Moreover, ROS levels were also influenced by copper. Under copper treatment, NO might play a protective role by regulating ROS levels possibly through modulation of the antioxidant activity.

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Studies on the cellular functions of newly discovered Prion family protein Shadoo

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The SPRN gene encodes the Shadoo glycoprotein (Sho), a central nervous system-expressed member of the prion protein super family. Sho is highly conserved from fish to mammals. SPRN is conserved in mammals, as is the prion gene PRNP, but in sheep SPRN and PRNP are both marked by polymorphic variation, suggestive of a shared selection pressure within these scrapie disease-prone livestock animals. In rodent models of prion disease there are reduced levels of Sho in infected tissues, defining a form of cross-regulation between full-length Sho holoprotein and PrP^{Sc}. The similarities between Sho and PrP N-terminus are the natively unfolded nature of polypeptide chains, a hydrophobic domain and tandem repeats with positively charged residues. Indeed, scrutiny of Sho's biochemical properties in uninfected cells has revealed overlaps with the properties of PrP^{C}, these including shared protein binding partners.

Prion protein functions as a metal binding protein because divalent cations such as copper, zinc and manganese can bind to the octapeptide repeat sequences in the N-terminus of PrP^{C}. Since the binding of these metals to the octapeptide has been proposed to influence both structural and functional properties of prion protein, alterations in transition metal levels can alter the course of the disease. As a member of the prion protein super family, we thought that Sho protein may behave like PrP as a metal binding protein, although it lacks the octapeptide region.

We carried out experiments on N2a cell lines stably expressing the Sho protein applying various concentrations of transition divalent metals. We could see the membrane internalisation of Sho protein induced by Co^{+2}, Mn^{+2} and Zn^{+2} ions. Also, we observed that the Sho expressing cells showed protection against the cytotoxic effects of Mn^{+2}.

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Identification and characterization of a novel circadian clock mutant in *Arabidopsis thaliana*

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The circadian clock is a biological timing mechanism that provides rhythmicity to gene expression, metabolism, and physiology with ~24h periodicity. The central oscillator of eukaryotic clocks is based on the network of clock genes and proteins, which are interconnected by transcriptional/translational negative feed-back loops.

Current models of the plant circadian clock postulate three interlocked feedback loops. A pair of single Myb-domain transcription factors, *CIRCADIAN CLOCK ASSOCIATED1 (CCA1)* and *LATE ELONGATED HYPOCOTYL (LHY)*, plays central roles in two loops. In one loop, *CCA1* and *LHY* repress the expression of the Pseudo-Response Regulator gene *TIMING OF CAB EXPRESSION 1 (TOC1)*. *TOC1* closes the first loop by inducing *CCA1* and *LHY* transcription for the next cycle. In a second loop, *PRR7* and *PRR9*, are induced by *CCA1* and *LHY*. *CCA1* and *LHY* are subsequently repressed by *PRR7* and *PRR9*. In a third loop, *GIGANTEA (GI)* and, possibly, *PRR5* are positive regulators of *TOC1*. *GI* is negatively regulated by both *CCA1/LHY* and *TOC1*.

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In order to identify novel components of the circadian system in *Arabidopsis thaliana*, we carried out a large-scale forward genetic screen. Several mutants, displaying altered rhythmic expression pattern of the *CAB2:LUC* reporter gene in continuous red light conditions, were isolated. The mutant *ct12* (*circadian time 12*) showed about 2 h period shortening under the screening conditions and was selected for further analysis. The mutation affected the expression of several clock-controlled genes in the same manner and the short period phenotype was independent of the light conditions. These findings indicated that the function of the core oscillator was altered in the mutant. In fact, expression of the core clock genes showed the expected short period phenotype, but the level of their expression was not affected significantly. This suggests that CT12 does not affect transcription of clock components directly. Consistent with the basic circadian dysfunction, *ct12* showed early flowering phenotype in short day conditions. We have provided experimental evidences that the flowering phenotype of the mutant is caused by the altered circadian period/phase. Moreover, *ct12* mutants produce long hypocotyls in red but not in blue light, suggesting a positive role for CT12 in light responses mediated by the red/far-red light absorbing phytochrome photoreceptors.

Genetic mapping followed by transgenic complementation showed that the *CT12* gene encodes a putative acyl-transferase. Although the exact biochemical function of this protein and the way it affects the function of the clock remains to be elucidated, we hypothesize that CT12 could represent a link between the clock and certain metabolic processes.

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The effect of recreational physical exercise on inflammatory markers in a rat model of colitis

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The sedentary lifestyle can lead to health problems such as metabolic syndrome including obesity with hypertension, insulin resistance and high blood lipid levels. Metabolic syndrome is associated with a chronic low-grade inflammatory state and oxidative stress. Many studies reported that physical activity is an effective way of controlling body weight, but the influence of long term low intensity exercise on inflammation and activity of anti- and proinflammatoric enzymes is not well known. Heme oxygenase-1 (HO-1), which is the inducible isoform of heme oxygenase enzyme (HO), is thought to play an important role in the protection of tissues from oxidative injuries. Another enzyme involved in oxidative stress and inflammation is nitric monoxide synthase enzyme (NOS) with 3 isoforms: the inducible (iNOS) and the two constitutively expressed (cNOS) isoforms namely neuronal NOS (nNOS) and endothelial NOS (eNOS). Nitric monoxide (NO) produced in different amount by the three NOS isoforms can be both harmful and beneficial. We used a rat model, trinitrobenzene-sulphonic acid (TNBS) induced colitis, to investigate the changes of inflammation and activity of HO and NOS enzymes in the colon after running.

We investigated the effects of long-term leisure-type physical exercise on the activity of HO, NOS and myeloperoxidase (MPO, an inflammatory marker) enzymes in the trinitrobenzene-sulphonic acid (TNBS) induced colitis in rats in dependence on time.

After 3, and 6 weeks self-administered physical activity (running wheel) male Wistar rats were treated with TNBS (10 mg). After 72 h TNBS challenge we measured colonic inflammatory parameters and HO, iNOS, cNOS, MPO activity.

While after 3-week running we found no difference in the severity and extent of colonic inflammation in the sedentary and running TNBS treated group, the 6-week freewheel running significantly increased the activity of HO (from 1,3±0,2 to 2,8±0,3 nmol bilirubin/h/mg protein), constitutive NOS isoforms (from 321,1±35,2 to 438,0±30,1 pmol/min/mg protein). The TNBS challenge after 6 weeks running significantly decreased the level of inflammatory markers including extent of lesions (from 54,6±2,6% to 42,9±3,2%), severity of mucosal damage (from 7,6±0,3 to 6,6±0,3) and the level of MPO activity (from 880,6±79,3 to 568,4±59,9 mU/mg protein), increased the activity of cNOS (from 108,9±25,6 to 333,9±32,3 pmol/min/mg protein) decreased the iNOS activity (from 217,6±26,4 to 128,9±15,8 pmol/min/mg protein), but did not changed the activity of HO compared to the sedentary TNBS-treated group.

Long lasting recreational physical activity, at least 6 weeks by rats, improves body's defence mechanisms. Physical activity-induced increasing activation of HO and cNOS systems, decreased activation of iNOS system may play role of these mechanisms including colonic inflammation.

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